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55-153P #7

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

APPLICANT : Tadashi MIYASAKA et al.

SERIAL NO. : 627,980

NOV 27 1985

FILED : July 5, 1984

GROUP 120

FOR : NEW CAMPTOTHECIN DERIVATIVES AND PROCESS FOR  
PREPARING SAME

Gibson

GROUP : 122

EXAMINER : Gibson

SUPPLEMENTAL RESPONSE

Commissioner of Patents  
and Trademarks  
Washington, D. C. 20231

November 27, 1985

Sir:

Further to the applicants' Amendment of October 31, 1985,  
the following supplemental remarks are respectfully submitted  
in connection with the above-identified application.

First of all, submitted herewith under 37 C.F.R. 1.132 is  
an executed Declaration by Dr. Masahiko Mutai which should be  
made a part of the record in this application. This  
Declaration reports the results of comparative tests between  
the compounds of the present invention and a comparative  
compound from the Miyasaka et al. reference cited by the

Examiner. The results of these comparative tests, as summarized in the table on page 7 of the Declaration, evidence the unexpected and improved activity for the presently claimed compounds and supports the patentability of the present invention.

Page 16 of applicants' previous Amendment filed on October 31, 1985 summarizes comparative test data for three compounds of the present invention and compound no. 4 taken from Miyasaka et al. However, subsequent to the filing of the October 31st Amendment, it was discovered that the test procedures utilized for obtaining the data for compound nos. 1-3 of the present invention were not the same as the procedure utilized for testing compound no. 4 of Miyasaka et al. Accordingly, the Examiner is requested to consider as the proper comparative test data that data presented in the herein submitted Declaration of Dr. Mutai, wherein the comparative test procedures for compound nos. 1-3 are the same as the procedure utilized for testing compound no. 4.

In further explanation of this matter, the Examiner is advised that the data set forth on page 16 of applicants' Amendment of October 31, 1985 was obtained by procedures wherein compound nos. 1-3 were administered to a test animal once a day for five consecutive days; whereas the procedure for

compound no. 4 comprised administering the test compound to a test animal on the first, fifth and ninth days after inoculation of the tumor cells. Thus the two procedures differed with respect to the number and days of administration of test compound. In the herein submitted Declaration by Dr. Mutai, however, compound nos. 1-4 were each administered to a test animal for five consecutive days following inoculation of tumor cells (see page 6 of the Declaration under the heading "Administration of the Test Compounds"). The procedures for obtaining the test results were, therefore, the same for each of the compounds; thereby providing a proper comparison between the compounds of the present invention (compound nos. 1-3) and the compound from Miyasaka et al. (compound no. 4).

Considering then the results of the comparative tests reported in the Mutai Declaration, Table 1 on page 7 of the Declaration presents the test results as follows:

Table 1

Compd. No.	Dose for the maximum T/C	T/C (%)	Number of mice alive for 40 days	TI
1	200 mg/kg	490	4/6	128(200/1.56)
2	100	424	3/6	128(200/1.56)
3	50	545	5/6	64(100/1.56)
4	150	190	0/6	50(150/3)

From the above, it is clear that the compounds of the present invention (compound nos. 1-3) show excellent activity as measured by the T/C values and especially as evidenced by the number of mice alive for 40 days as compared with the compound of Miyasaka et al. (compound no. 4).

In view of the above, taken together with the Mutai Declaration submitted herewith and the amendments and remarks submitted with applicants' Amendment of October 31, 1985, it is believed that the applicants have shown that the compounds of the present invention are structurally distinguishable from those of Miyasaka et al. and exhibit unexpected and improved activity as compared to the Miyasaka et al. compounds. Accordingly, reconsideration and withdrawal of the rejections and early allowance of all the claims are earnestly solicited.

Please charge any fees or credit any overpayment pursuant to 37 C.F.R. 1.16 or 1.17 to Deposit Account 02-2448.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH

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Enclosure